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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/670,504	09/26/2003	Steven Leigh	032553-037	8609

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EXAMINER	
KISHORE, GOLLAMUDI S	
ART UNIT	PAPER NUMBER
1615	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/08/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/670,504	LEIGH ET AL.	
	Examiner	Art Unit	
	Gollamudi S. Kishore, Ph.D	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-22 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-22 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date 4-1-04.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is confusing since it is unclear as to whether applicant is claiming a single composition or two compositions to prepare a single composition. The examiner is interpreting the claim as a single composition. The preamble on line 1 says 'a composition for mixing'. It is unclear as to what it is mixed with. The distinction between 'membrane lipid' in A and lipids in B in claim 1 and 13 is unclear. Furthermore, it is unclear as to what applicant intends to convey by 'membrane lipid'. Lipids form biological membranes or lipids, which form liposomes? The use of trade name 'Cremophor EL' is improper. The examiner suggests the use of chemical name.

According to claim 13, the first container contains the water miscible solvent; claim 19, which recites that the content of container A is an amorphous powder, is inconsistent with claim 13.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

4. Claims 1-5 and 9-12 are rejected under 35 U.S.C. 102(a) as being anticipated by WO 00/16770 of record.

WO discloses compositions containing paclitaxel, a triglyceride of fatty acids with 2-22 carbon atoms (triacetin or tributynin), a phospholipid, fatty acid salts and water miscible glycerol. Although WO does not teach the liposomal sizes before the addition, since the composition is a single composition and since it teaches the final particle sizes, in the absence of showing otherwise, the reference meets the requirements of instant claims. (abstract and Examples, Examples 1-4 in particular in WO and English translation).

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

5. Claims 1-3, 6, 12-16 and 20-22 are rejected under 35 U.S.C. 102(e) as being anticipated by Watts et al (6,383,513).

Watts et al disclose a composition containing a water insoluble cannabinoid, ethanol, sesame oil (membrane lipid) and egg yolk phospholipid and a method of preparation. The method involves combining the cannabinoid, ethanol, and oil solution to aqueous dispersion of phospholipid (Example 6). Since liposomes are formed spontaneously when the phospholipids are hydrated with and aqueous medium, the reference meets the requirements of instant claim 7.

The examiner cites the reference of Mehta, which shows that the addition of an aqueous medium to a phospholipid would result in the formation of liposomes (Example 1).

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1-12 are rejected under 35 U.S.C. 102(b) as being anticipated by Weder (5,997,888).

Weder discloses nanodispersions containing an oil soluble active agent, Tween 80, ethanol and at least one phospholipid. The particles have sizes smaller than 60 nm (abstract, col. 2, line 20 through col. 4, line 12; col. 4, line 50 through col. 6,line 64; Examples and claims). The reference meets the requirements of instant claims.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 4-10, 12, 16-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Watts et al.

The teachings of Watts et al have been discussed above. Watts et al do not specifically disclose that the phospholipid in the aqueous suspension is in the form of liposomes or in the claimed sizes. As pointed out above, since the art known method for the preparation of liposomes is the addition of an aqueous medium to the phospholipid

to hydrate it, which results in the formation of liposomes, it is implicit that the aqueous suspension taught by Watts is in the form of liposomes. Watts et al do not teach the sizes of the liposomes before mixing with the active agent in ethanol. Watts et al also do not teach high-pressure homogenization and extrusion of the aqueous suspension of the phospholipid before mixing. However, Watt et al do teach the homogenization and extrusion of the composition after the addition of the two phases. Therefore, in the absence of showing unexpected results, the steps of homogenization and extrusion of the composition before or after the addition of the two phases are deemed to be manipulatable parameters practiced by an artisan to obtain the best possible results. Watts et al also do not teach the inclusion of a phospholipid in the ethanol phase. However, since the final product contains the phospholipid, the criticality of the addition of the phospholipid in the ethanol phase also is unclear to the examiner.

9. Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Watts et al or Weder cited above, further in view of Leigh (5,004,611).

The teachings of Watts et al and Weder have been discussed above. Both Watts et al and Weder teach the use of ethanol, but not glycerol. The use of glycerol instead of ethanol would have been obvious to one of ordinary skill in the art with a reasonable expectation of success since Leigh teaches that either can be used for the preparation of liposomes (col. 3, lines 50-56).

10. Claims 1-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Janoff et al (5,616,334) in combination with Leigh (5,004,611).

Janoff teaches a method of encapsulation of water insoluble drugs such as amphotericin B. The method involves adding the ethanolic solutions of the drug to liposomal suspension in an aqueous medium. The liposomal sizes can vary from sizes of 0.2 microns (col. 5, lines 24-43; col. 15, lines 1-9, Example 9).

What is lacking in Janoff is the inclusion of a surfactant in the ethanolic solution.

Leigh while disclosing liposomal formulations teaches that the inclusion of surfactants such as sorbitans sold as SPANS increases the entrapment efficiency and also strengthens the liposomes in some way (abstract and col. 5, lines 1-12).

The inclusion of a surfactant in the method of loading an active agent taught by Janoff and prepare a composition containing a water insoluble active agent would have been obvious to one of ordinary skill in the art since such an inclusion would increase the entrapment efficiency and also strengthen the liposomes as taught by Leigh.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gollamudi S. Kishore, Ph.D whose telephone number is (571) 272-0598. The examiner can normally be reached on 6:30 AM- 4 PM, alternate Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Woodward Michael can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Gollamudi S Kishore, Ph.D
Primary Examiner
Art Unit 1615

GSK